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(74) Agent: KAGAN, Sarah, A.; Banner & Witcoff, Ltd., 11th floor, 1001 G Street, N.W., Washington, DC 20001-4597 (US).

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(71) Applicant (*for all designated States except US*): THE JOHN HOPKINS UNIVERSITY [US/US]; 3400 N. Charles Street, Baltimore, MD 21218 (US).

(72) Inventors; and

(75) Inventors/Applicants (*for US only*): WANG, Tian-LI [US/US]; 5208 Springlake Way, Baltimore, MD 21212 (US). DIAZ, Luis [US/US]; 5943 Meadow Rose, Eldridge, MD 21075 (US). LENGAUER, Christoph [AT/US]; 9212 Adalee Court, Columbia, MD 21045 (US). VELCULESCU, Victor [US/US]; 14064 Big Branch Drive, Dayton, MD 21036 (US). KINZLER, Kenneth, W. [US/US]; 1403 Halkirk Way, Bel Air, MD 21015 (US). VOGELSTEIN, Bert [US/US]; 3700 Breton Way, Baltimore, MD 21208 (US).

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(54) Title: THYMIDYLATE SYNTHASE GENE AND METASTASIS

(57) Abstract: Thymidylate synthase (TYMS) gene amplification was observed in 23% of 31 5-FU resistant liver metastases, while no amplification was observed in metastases of patients that had not been treated with 5-FU. Patients with metastases containing TYMS amplification had a substantially shorter median survival (329 days) than those without amplification (1021 days,  $p < 0.01$ ). Genetic amplification of TYMS has important implications for the management of colorectal cancer patients with recurrent disease.



WO 2005/076984 A3

# INTERNATIONAL SEARCH REPORT

International Application No.

PCT/US05/03776

## A. CLASSIFICATION OF SUBJECT MATTER

IPC: C07H 21/04( 2006.01);C12Q 1/68( 2006.01)

USPC: 435/6;536/23.1

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 435/6; 536/23.1

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
TS, thymidylate; 5-FU,

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	GORLICK et al. "Higher levels of thymidylate synthase gene expression oare observed in pulmonary as compared with hepatic metastases of colorectal adenocarcinoma." J. of Clinical Oncology, Vol. 16, No. 4, pages 1465-1469, April 1998.	1-3, 5-9, 13-15 ----- 4-5, 10-12, 16-20
X	HIDAKA et al. Rinsho Byori, Vol. 199, pages 164-170, 2002.	1, 3-5
Y	ROONEY et al. "Comparative genomic hybridization analysis of choromsosomal alterations induced by the development of resistance to thymidylate synthase inhibitors." Cancer Reserach, Vol. 58, pages 5042-5045, November 15, 1998.	4-5
Y	HIDAKA et al. "Chromosomal imbalances associated with acquired resistance to fluoropyrimidines in human colorectal cancer cells." Eur. J. of Cancer. Vol. 39, pages 975-980, 2003.	10-12, 16-20

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☐ See patent family annex.

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"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family
"P" document published prior to the international filing date but later than the priority date claimed	

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Mail Stop PCT, Attn: ISA/US  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, Virginia 22313-1450

Facsimile No. (571) 273-3201

Authorized officer

Jeanine Enewold Goldberg

Telephone No. (571)-272-1600

*J. Goldberg*